

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date  
3 March 2005 (03.03.2005)

PCT

(10) International Publication Number  
**WO 2005/018565 A2**

(51) International Patent Classification<sup>7</sup>:

A61K

(21) International Application Number:

PCT/US2004/027156

(22) International Filing Date: 18 August 2004 (18.08.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/560,748 21 August 2003 (21.08.2003) US  
60/598,672 3 August 2004 (03.08.2004) US

(71) Applicant (for all designated States except US): TRANSORAL PHARMACEUTICALS, INC. [US/US]; 300 Tamal Plaza, Suite 220, Corte Madera, CA 94925 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only): SINGH, Nikhilesh, N. [US/US]; 1220 Shelter Bay Avenue, Mill Valley, CA 94941 (US).

(74) Agents: KEZER, William, B. et al.; Townsend and Townsend and Crew LLP, Two Embarcadero Center, 8th Floor, San Francisco, CA 94111-3834 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

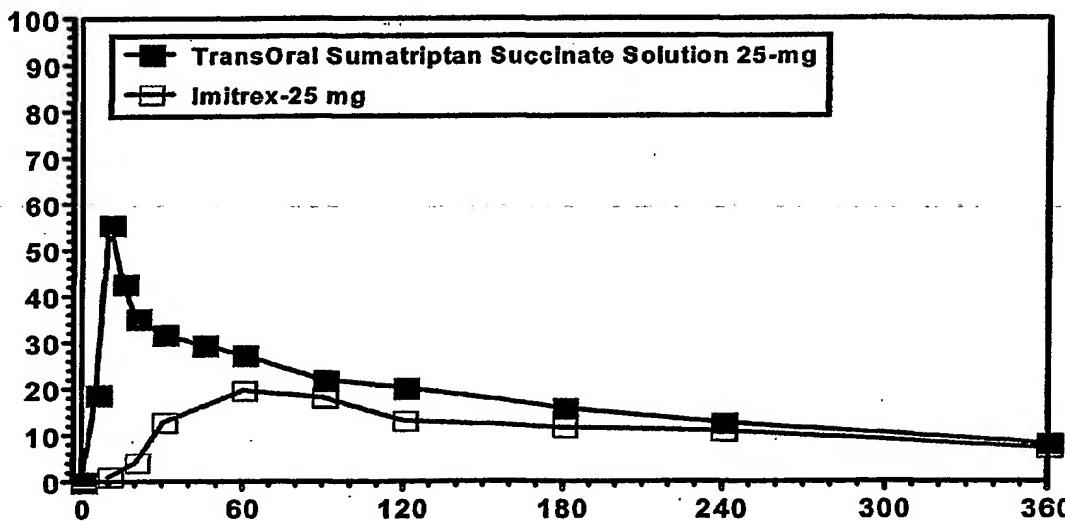
(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished upon receipt of that report

[Continued on next page]

(54) Title: COMPOSITIONS FOR DELIVERING 5-HT AGONISTS ACROSS THE ORAL MUCOSA AND METHODS OF USE THEREOF



(57) Abstract: The present invention provides novel compositions for the delivery of a 5-hydroxytryptamine (5-HT) agonist across the oral mucosa. In particular, the buffer system in the compositions of the present invention raises the pH of saliva to a pH greater than about 9.9, thereby facilitating the substantially complete conversion of the 5-HT agonist from its ionized to its un-ionized form. As a result, the dose of 5-HT agonist is rapidly and efficiently absorbed by the oral mucosa. Furthermore, delivery of the 5-HT agonist across the oral mucosa advantageously bypasses hepatic first pass metabolism of the drug and avoids enzymatic degradation of the drug within the gastrointestinal tract. Methods for using the compositions of the present invention for treating migraines are also provided.

WO 2005/018565 A2



*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date  
3 March 2005 (03.03.2005)

PCT

(10) International Publication Number  
**WO 2005/018565 A3**

(51) International Patent Classification<sup>7</sup>: **A61K 7/16**

(21) International Application Number:  
**PCT/US2004/027156**

(22) International Filing Date: 18 August 2004 (18.08.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/560,748 21 August 2003 (21.08.2003) US  
60/598,672 3 August 2004 (03.08.2004) US

(71) Applicant (for all designated States except US): TRAN-SORAL PHARMACEUTICALS, INC. [US/US]; 300 Tamal Plaza, Suite 220, Corte Madera, CA 94925 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only): SINGH, Nikhilesh, N. [US/US]; 1220 Shelter Bay Avenue, Mill Valley, CA 94941 (US).

(74) Agents: KEZER, William, B. et al.; Townsend and Townsend and Crew LLP, Two Embarcadero Center, 8th Floor, San Francisco, CA 94111-3834 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:  
2 June 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

**WO 2005/018565 A3**

(54) Title: COMPOSITIONS FOR DELIVERING 5-HT AGONISTS ACROSS THE ORAL MUCOSA AND METHODS OF USE THEREOF

(57) Abstract: The present invention provides novel compositions for the delivery of a 5-hydroxytryptamine (5-HT) agonist across the oral mucosa. In particular, the buffer system in the compositions of the present invention raises the pH of saliva to a pH greater than about 9.9, thereby facilitating the substantially complete conversion of the 5-HT agonist from its ionized to its un-ionized form. As a result, the dose of 5-HT agonist is rapidly and efficiently absorbed by the oral mucosa. Furthermore, delivery of the 5-HT agonist across the oral mucosa advantageously bypasses hepatic first pass metabolism of the drug and avoids enzymatic degradation of the drug within the gastrointestinal tract. Methods for using the compositions of the present invention for treating migraines are also provided.